Complete Summary

GUIDELINE TITLE

Prevention of venous thromboembolism. In: Sixth ACCP Consensus Conference on Antithrombotic Therapy.

BIBLIOGRAPHIC SOURCE(S)

Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA Jr, Wheeler HB. Prevention of venous thromboembolism. Chest 2001 Jan;119(1 Suppl):132S-175S. [630 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Venous thromboembolism

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Family Practice
Internal Medicine
Neurological Surgery
Obstetrics and Gynecology
Orthopedic Surgery
Preventive Medicine

Pulmonary Medicine
Surgery
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To review the literature related to the risks of venous thromboembolism and its prevention
- To recommend evidence-based prophylaxis strategies for the prevention of venous thromboembolism

TARGET POPULATION

1. Patients undergoing surgery, such as:
    - Major general, gynecologic, and urologic surgery
    - Lower extremity arthroplasty and hip fracture repair
    - Neurosurgery
    - Elective spine surgery
2. Patients admitted to the hospital with major trauma, spinal cord injury, lower extremity fractures, or burns.
3. Medical patients with risk factors for thromboembolism, including:
    - Myocardial infarction
    - Ischemic stroke
    - Other medical conditions, such as cancer, bedrest, heart failure, or severe lung disease
    - Critical care

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention of Venous Thromboembolism:

1. Assessment of clinical risk factors for venous thromboembolism
2. Selective screening for venous thromboembolism with duplex ultrasonography
3. Non-pharmacologic prophylaxis measures:
    a. Early ambulation or mobilization
    b. Mechanical prophylaxis, such as elastic (graduated compression) stockings, intermittent pneumatic compression or venous foot pumps)
4. Pharmacologic prophylaxis:
    a. Heparin therapy; low-dose unfractionated heparin; low-molecular-weight heparin; adjusted-dose heparin therapy; heparinoid, such as danaparoid
    b. Adjusted-dose oral anticoagulation

    Note: Aspirin and dextran were considered for prophylaxis but not recommended for any patient group.

5. Selected inferior vena cava filter insertion for demonstrated proximal deep vein thrombosis in the presence of a contra-indication to therapeutic anticoagulation

MAJOR OUTCOMES CONSIDERED

- Efficacy of prophylactic strategies for venous thromboembolism
- Rates and relative risk of venous thromboembolism outcomes, such as:
    - Fatal pulmonary embolism
    - Symptomatic, proven deep vein thrombosis or pulmonary embolism
    - Asymptomatic proximal deep vein thrombosis
- Cost effectiveness of prophylaxis

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The participants reviewed information from an exhaustive review of the literature.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) (see "Rating Scheme for the Strength of the Recommendations") and the methodologic quality of the underlying evidence (A, B, C+, or C).

Grades of evidence for antithrombotic agents:

1A
Methodological strength of supporting evidence: randomized controlled trials without important limitations

1B
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)

1C+
Methodological strength of supporting evidence: no randomized controlled trials, but randomized controlled trial results can be unequivocally extrapolated; or, overwhelming evidence from observational studies

1C
Methodological strength of supporting evidence: observation studies

2A
Methodological strength of supporting evidence: randomized controlled trials without important limitations

2B
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)

2C
Methodological strength of supporting evidence: observational studies

* Such situations include randomized controlled trials with lack of blinding, and subjective outcomes, in which the risk of bias in measurement of outcomes is high; and randomized controlled trials with large loss to follow-up.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The rates of deep vein thrombosis were pooled in summary tables from the eligible trials for each intervention and then compared with the rate among pooled, untreated, or placebo-treated control patients to determine the reduction in relative risk.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The strength of any recommendation depends on two factors: the trade-off between benefits and risks, and the strength of the methodology that leads to estimates of the treatment effect. The rating scheme used for this guideline captures these factors. The guideline developers grade the trade-off between benefits and risks in two categories: (1) the trade-off is clear enough that most patients, despite differences in values, would make the same choice; and (2) the trade-off is less clear, and each patient's values will likely lead to different choices.

When randomized trials provide precise estimates suggesting large treatment effects, and risks and costs of therapy are small, treatment for average patients with compatible values and preferences can be confidently recommended. If the balance between benefits and risks is uncertain, methodologically rigorous studies providing grade A evidence and recommendations may still be weak (grade 2). Uncertainty may come from less precise estimates of benefit, harm, or costs, or from small effect sizes.

There is an independent impact of validity/consistency and the balance of positive and negative impacts of treatment on the strength of recommendations. In situations when there is doubt about the value of the trade-off, any recommendation will be weaker, moving from grade 1 to grade 2.

Grade 1 recommendations can only be made when there are precise estimates of both benefit and harm, and the balance between the two clearly favors recommending or not recommending the intervention for the average patient with compatible values and preferences. Table 2 of the original guideline document summarizes how a number of factors can reduce the strength of a recommendation, moving it from grade 1 to grade 2. Uncertainty about a recommendation to treat may be introduced if the target event that is trying to be prevented is less important (confident recommendations are more likely to be made to prevent death or stroke than asymptomatic deep venous thrombosis); if the magnitude of risk reduction in the overall group is small; if the risk is low in a particular subgroup of patients; if the estimate of the treatment effect, reflected in a wide confidence interval (CI) around the effect, is imprecise; if there is substantial potential harm associated with therapy; or if there is an expectation for a wide divergence in values even among average or typical patients. Higher costs would also lead to weaker recommendations to treat.

The more balanced the trade-off between benefits and risks, the greater the influence of individual patient values in decision making. If they understand the benefits and risks, virtually all patients will take aspirin after myocardial infarction or will comply with prophylaxis to reduce thromboembolism after hip replacement. Thus, one way of thinking about a grade 1 recommendation is that variability in patient values or individual physician values is unlikely to influence treatment choice in average or typical patients.

When the trade-off between benefits and risks is less clear, individual patient values will influence treatment decisions even among patients with average or typical preferences.

Grade 2 recommendations are those in which variation in patient values or individual physician values will often mandate different treatment choices, even among average or typical patients.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodologic quality of the underlying evidence (A, B, C+, or C) (see "Rating Scheme for the Strength of the Evidence").

Grades of recommendation for antithrombotic agents:

1A
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; can apply to most circumstances, without reservation

1B
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; likely to apply to most patients

1C+
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; can apply to most patients in most circumstances

1C
Clarity of risk/benefit: risk/benefit clear
Implications: intermediate-strength recommendation; may change when stronger evidence available

2A
Clarity of risk/benefit: risk/benefit unclear
Implications: intermediate strength recommendation; best action may differ, depending on circumstances or patients' societal values

2B
Clarity of risk/benefit: risk/benefit unclear
Implications: weak recommendation; alternative approaches likely to be better for some patients under some circumstances

2C
Clarity of risk/benefit: risk/benefit unclear
Implications: very weak recommendation; other alternatives may be equally reasonable

COST ANALYSIS

The costs of thromboprophylaxis have been used as an argument against its wider use; however, the studies addressing this issue have uniformly concluded that broad application of prophylaxis is highly cost-effective.

General Surgery

Given the approximate equivalence in efficacy and safety of low-dose unfractionated heparin (LDUH) and low-molecular-weight heparin (LMWH) in general surgery patients, cost becomes an important determinant in the choice between these drugs. In North America, LMWHs cost 2 to 10 times more than LDUH, and the cost-effectiveness analyses performed in abdominal and colorectal surgery patients concluded that prophylaxis with LDUH was more economical. In countries where LMWHs are less expensive, these agents may be equivalent in overall costs and more appealing because of once daily administration.

The issue of prophylaxis beyond the period of hospitalization was addressed in a single small, randomized study of high-risk patients undergoing major abdominal or thoracic surgery. Prolonged prophylaxis with LMWH for 3 weeks after hospital discharge did not significantly reduce the incidence of DVT as assessed by bilateral venography performed 4 weeks after surgery, compared with 1 week of in-hospital LMWH (5% vs 10%). However, a total of only 118 patients had adequate venography. A cost-effectiveness analysis, based on event rates from the literature, concluded that postdischarge prophylaxis of general surgery patients was effective, but the marginal costs were too high to warrant its routine use. The issue of duration of thromboprophylaxis in general surgery must now be reevaluated in the context of current short lengths of hospital stay.

Gynecologic Surgery

Use of elastic (graduated compression) stockings (ES) or intermittent pneumatic compression (IPC) is likely to be efficacious in urosurgery, but the high costs of intermittent pneumatic compression have been raised as a problem with this method. It is also possible that the addition of intermittent pneumatic compression to inexpensive of elastic (graduated compression) stockings may not provide additional protection in these patients. However, combining mechanical and pharmacologic prophylaxis may be more effective than either alone but will substantially increase the costs.

The benefits of any prophylaxis regimen should be weighed against the costs, including those resulting from bleeding complications, as well as the costs associated with failed prophylaxis (e g., VTE and death). This comparison is best performed using a formal cost-effectiveness analysis. Although the guideline developers report cost-effectiveness studies where available, they should be interpreted with caution, as most used risk reduction in asymptomatic DVT by venography to determine the potential benefit derived from each prophylaxis regimen.

Elective Total Hip Replacement (THR) Surgery

Withholding primary prophylaxis in favor of case-finding by serial noninvasive screening for asymptomatic DVT is problematic in this patient population because the commonly available noninvasive tests (impedance plethysmography or compression or color duplex ultrasonography) are insensitive for asymptomatic calf and proximal DVT. Moreover, clinical trials and cohort studies have found that a strategy of screening for proximal DVT with predischarge color duplex ultrasonography was ineffective. While a similar strategy using predischarge venography appeared to be cost-effective in a single study, routine venography is not widely available or generally acceptable.

Elective Total Knee Replacement (TKR) Surgery

Similar to total hip replacement, the guideline developers suggest that the choice of LMWH or warfarin prophylaxis for total knee replacement surgery be an institutional decision. The overall costs of utilizing warfarin or LMWH prophylaxis following lower extremity arthroplasty are similar. In a recent analysis based on US health-care costs, adjusted-dose warfarin prophylaxis was slightly more cost-effective than LMWH.

Trauma

Greenfield has estimated the cost of prophylactic IVC filter insertions to be $900,000,000 per year if they were placed in only 1% of disabling trauma patients. Finally, PE and occasional fatal PE still occur despite the presence of a filter. When LMWH is used as prophylaxis, the addition of screening with duplex scanning or the insertion of a vena caval filter has been estimated to cost > $100,000 per PE prevented. Another analysis concluded that routine screening or prophylactic vena caval filter insertion would not prevent any deaths or otherwise benefit trauma patients. There is insufficient evidence to recommend the prophylactic insertion of IVC filters in trauma patients, even in those at high risk for VTE, and a more conservative approach to its use is emerging. IVC filter insertion is primarily indicated for patients with proven proximal DVT and who have absolute contraindications to full anticoagulation or require major surgery in the near future.

Cancer patients

Rajan et al performed a cost-effectiveness analysis using the results of a randomized trial performed by Levine et al and showed that very low dose warfarin can be provided to women with metastatic breast cancer receiving chemotherapy without an increase in health-care costs.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The initial guidelines were prepared by the chapter committee (the primary authors) and then reviewed separately by the Committee Co-Chairs and methodology experts and finally by the entire group of Consensus Guideline participants.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Please note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary. The recommendations that follow are based on the previous version of the guideline.

Excerpted by the National Guideline Clearinghouse (NGC):

The grading scheme is defined at the end of the Major Recommendations.

General Recommendations

1. The guideline developers recommend that every hospital develop a formal strategy that addresses the prevention of thromboembolic complications. This

should generally be in the form of a written thromboprophylaxis policy especially for high-risk groups.
2. For all patient groups, the guideline developers do not recommend aspirin for prophylaxis, because other measures are more efficacious (grade 1A).
3. In all patients having spinal puncture or epidural catheters placed for regional anesthesia or analgesia, the guideline developers recommend that antithrombotic therapy or prophylaxis be used with caution (grade 1C+).

Surgery

General Surgery

1. In low-risk general surgery patients (see Table 2 in the original guideline document) who are undergoing minor procedures, are <40 years of age, and have no additional risk factors, the guideline developers recommend the use of no specific prophylaxis other than early ambulation (grade 1C).
2. Moderate-risk general surgery patients are those undergoing minor procedures but have additional thrombosis risk factors, those having nonmajor surgery between the ages of 40 and 60 years with no additional risk factors, or those undergoing major operations who are younger than 40 years with no additional clinical risk factors. The guideline developers recommend prophylaxis with low-dose unfractionated heparin, low-molecular-weight heparin, elastic (graduated compression) stockings, or intermittent pneumatic compression (all grade 1A in comparison to no prophylaxis).
3. Higher-risk general surgery patients are those having nonmajor surgery over the age of 60 years or with additional risk factors or patients undergoing major surgery over the age of 40 years or with additional risk factors. The guideline developers recommend thrombosis prophylaxis with low-dose unfractionated heparin, low-molecular-weight heparin, or intermittent pneumatic compression (all grade 1A in comparison to no prophylaxis).
    - In higher-risk general surgery patients with a greater than usual risk of bleeding, the guideline developers recommend the use of mechanical prophylaxis with elastic (graduated compression) stockings or intermittent pneumatic compression, at least initially (grade 1C).
4. In very-high-risk general surgery patients with multiple risk factors, the guideline developers recommend that effective pharmacologic methods (low-dose unfractionated heparin or low-molecular-weight heparin) be combined with elastic (graduated compression) stockings or intermittent pneumatic compression (grade 1C based on small studies and on extrapolation of data from other patient groups).
5. In selected very-high-risk general surgery patients, the guideline developers recommend that clinicians consider postdischarge low-molecular-weight heparin or perioperative warfarin (international normalized ratio 2.0 to 3.0) (grade 2C).

Gynecologic Surgery

1. For gynecologic surgery patients undergoing brief procedures for benign disease, the guideline developers recommend early mobilization alone (grade 1C).
2. The guideline developers recommend that patients having major gynecologic surgery for benign disease, without additional risk factors, receive twice daily

low-dose unfractionated heparin (grade 1A). Alternatives include once daily low-molecular-weight heparin or intermittent pneumatic compression, started just before surgery and continued for at least several days postoperatively (grade 1C+).
3. For patients undergoing extensive surgery for malignancy, the guideline developers recommend routine prophylaxis with three daily doses of low-dose unfractionated heparin (grade 1A). Alternative considerations include the combination of low-dose unfractionated heparin plus mechanical prophylaxis with elastic (graduated compression) stockings or intermittent pneumatic compression, or higher doses of low-molecular-weight heparin, since these options may provide additional protection (grade 1C).

Urologic Surgery

1. In patients undergoing transurethral or other low-risk urologic procedures, the guideline developers recommend that no specific prophylaxis other than prompt ambulation be used (grade 1C).
2. For patients with major, open urologic procedures, the guideline developers recommend routine prophylaxis with low-dose unfractionated heparin, elastic (graduated compression) stockings, intermittent pneumatic compression, or low-molecular-weight heparin (all grade 1B in comparison to no prophylaxis).
3. For patients at the highest risk, the guideline developers recommend combining elastic (graduated compression) stockings plus or minus intermittent pneumatic compression, with low-dose unfractionated heparin or low-molecular-weight heparin (grade 1C).

Elective Hip Replacement

1. For patients undergoing elective total hip replacement surgery, the guideline developers recommend either subcutaneous low-molecular-weight heparin therapy (started 12 hours before surgery, 12 to 24 hours after surgery, or 4–6 hours after surgery at half the usual high-risk dose and then continuing with the usual high-risk dose the following day), or adjusted-dose warfarin (international normalized ratio target = 2.5, range 2.0 to 3.0; started preoperatively or immediately after surgery) (all grade 1A).
2. Adjusted-dose heparin therapy (started preoperatively) is an acceptable but more complex alternative (grade 2A).
3. Adjuvant prophylaxis with elastic (graduated compression) stockings or intermittent pneumatic compression may provide additional efficacy (grade 2C).
4. Although other agents such as low-dose unfractionated heparin, aspirin, dextran, and intermittent pneumatic compression alone may reduce the overall incidence of venous thromboembolism, they are less effective, and the guideline developers do not recommend that these options be used.

Elective Knee Replacement

1. For patients undergoing elective total knee replacement surgery, the guideline developers recommend either low-molecular-weight heparin or adjusted-dose warfarin (grade 1A).

2. Optimal use of intermittent pneumatic compression is an alternative option (grade 1B recommendation because of the few trials and small sample sizes).
3. Low-dose unfractionated heparin is not recommended (grade 1C+).

Hip Fracture Surgery

1. For patients undergoing hip fracture surgery, the guideline developers recommend either low-molecular-weight heparin or adjusted-dose warfarin prophylaxis (grade 1B because the available data are limited).
2. The use of low-dose unfractionated heparin may be an alternative option, but this is a grade 2B recommendation based on the very limited available data.
3. The guideline developers do not recommend the use of aspirin alone because it is less efficacious than other approaches (grade 2A).

Other Prophylaxis Issues for Major Orthopedic Surgery

1. The optimal duration of anticoagulant prophylaxis after total hip replacement or total knee replacement surgery is uncertain, although at least 7 to 10 days of prophylaxis is recommended (grade 1A).
2. Extended out-of-hospital low-molecular-weight heparin prophylaxis (beyond 7 to 10 days after surgery) may reduce the incidence of clinically important thromboembolic events, and the guideline developers recommend this approach at least for high-risk patients (grade 2A because of uncertainty regarding cost-effectiveness).
3. The guideline developers do not recommend routine duplex ultrasonography screening at the time of hospital discharge or during outpatient follow-up in asymptomatic total hip replacement or total knee replacement patients (grade 1A).

Neurosurgery, Trauma, and Acute Spinal Cord Injury

Neurosurgery

1. The guideline developers recommend the use of intermittent pneumatic compression with or without elastic (graduated compression) stockings in patients undergoing intracranial neurosurgery (grade 1A).
2. Low-dose unfractionated heparin or postoperative low-molecular-weight heparin are acceptable alternatives (grade 2A because of concerns about clinically important intracranial hemorrhage).
3. The combination of physical (elastic stockings or intermittent pneumatic compression) and pharmacologic (low-molecular-weight heparin or low-dose unfractionated heparin) prophylaxis modalities may be more effective than either modality alone in high-risk patients (grade 1B).

Trauma

1. Trauma patients with an identifiable risk factor for thromboembolism should receive prophylaxis if possible. If there is no contraindication, the guideline developers recommend that clinicians use low-molecular-weight heparin, starting treatment as soon as it is considered safe to do so (grade 1A).

2. The guideline developers recommend that initial prophylaxis with a mechanical modality (elastic stockings and/or intermittent pneumatic compression) be used if low-molecular-weight heparin prophylaxis will be delayed or is contraindicated because of concerns about the patient´s risk of bleeding (grade 1C).
3. In patients at high risk for thromboembolism who have received suboptimal prophylaxis, consideration should be given to screening with duplex ultrasound (grade 1C).
4. The guideline developers recommend that inferior vena cava filter insertion be used if proximal deep vein thrombosis is demonstrated and anticoagulation is contraindicated (grade 1C+). The guideline developers do not recommend the use of inferior vena cava filter insertion for primary prophylaxis (grade 1C).

Acute Spinal Cord Injury

1. In patients with acute spinal cord injury, the guideline developers recommend prophylaxis with low-molecular-weight heparin (grade 1B).
2. Low-dose unfractionated heparin, elastic (graduated compression) stockings, and intermittent pneumatic compression appear to be relatively ineffective when used alone, and the guideline developers do not recommend these modalities (grade 1C).
3. Elastic (graduated compression) stockings and intermittent pneumatic compression might have benefit if used in combination with low-molecular-weight heparin or low-dose unfractionated heparin or if anticoagulants are contraindicated early after injury (grade 2B).
4. In the rehabilitation phase of acute spinal cord injury, the guideline developers recommend the continuation of low-molecular-weight heparin therapy or conversion to full-dose oral anticoagulation (international normalized ratio target 2.5, range 2.0 to 3.0) (grade 1C).

Medical Conditions

Acute Myocardial Infarction

1. The guideline developers recommend that most patients with acute myocardial infarction receive prophylactic or therapeutic anticoagulant therapy with subcutaneous low-dose unfractionated heparin or intravenous heparin (grade 1A).

Ischemic Stroke

1. For patients with ischemic stroke and impaired mobility, the guideline developers recommend the routine use of low-dose unfractionated heparin, low-molecular-weight heparin, or the heparinoid, danaparoid (all grade 1A).
2. If anticoagulant prophylaxis is contraindicated, the guideline developers recommend mechanical prophylaxis with elastic (graduated compression) stockings or intermittent pneumatic compression (grade 1C+).

Other Medical Conditions

1. In general medical patients with risk factors for venous thromboembolism (including cancer, bedrest, heart failure, severe lung disease), the guideline developers recommend low-dose unfractionated heparin or low-molecular-weight heparin (grade 1A).

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodologic quality of the underlying evidence (A, B, C+, or C).

Definitions:

Grades of recommendations:

1A

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: randomized controlled trials without important limitations
Implications: strong recommendation; can apply to most circumstances, without reservation

1B

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)
Implications: strong recommendation; likely to apply to most patients

1C+

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: no randomized controlled trials, but randomized controlled trial results can be unequivocally extrapolated; or, overwhelming evidence from observational studies
Implications: strong recommendation; can apply to most patients in most circumstances

1C

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: observation studies
Implications: intermediate-strength recommendation; may change when stronger evidence available

2A

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: randomized controlled trials without important limitations
Implications: intermediate strength recommendation; best action may differ, depending on circumstances or patients' societal values

2B

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)
Implications: weak recommendation; alternative approaches likely to be better for some patients under some circumstances

2C

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: observational studies
Implications: very weak recommendation; other alternatives may be equally reasonable

* Such situations include randomized controlled trials with lack of blinding, and subjective outcomes, in which the risk of bias in measurement of outcomes is high; and randomized controlled trials with large loss to follow-up.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified for each recommendation (refer to "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate prevention strategies for venous thromboembolism may lead to:

- Decreased rates and relative risk of deep vein thrombosis and other adverse venous thromboembolism outcomes including pulmonary embolism and fatal pulmonary embolism
- Decreased health care costs. Studies addressing cost have uniformly concluded that broad application of prophylaxis is highly cost-effective

Subgroups Most Likely to Benefit:

The guideline developers have described four levels of thromboembolism risk and summarized the successful prophylaxis strategies (see Table 2 in the original guideline document). For each of the major patient groups, the guideline developers discuss recommendations for average-risk and higher-risk patients. In general, the patients most likely to benefit from the guidelines are those in the higher risk groups (these groups will have the lowest number-needed-to-treat).

POTENTIAL HARMS

Adverse effects of pharmacologic agents may occur, including:

- Bleeding complications from anticoagulants.
- Heparin-induced thrombocytopenia. The rate of thrombocytopenia with prophylactic use of heparin is 1 to 5%, and the incidence of clinically overt vascular thrombosis in postoperative patients with heparin-induced thrombocytopenia is approximately 50%. Low-molecular-weight heparins are much less likely to produce heparin-induced thrombocytopenia than unfractionated heparin.
- Wound hematomas, which are seen more frequently with low-dose unfractionated heparin or low-molecular-weight heparin than with mechanical or no prophylaxis or, in some studies, than oral anticoagulation. These agents may potentially increase the risk of wound infection, dehiscence, and infection of a prosthetic device placed at the time of operation.
- Perispinal hematoma after neuraxial blockade (spinal or epidural anesthesia or epidural analgesia). This is a rare but serious complication of anticoagulant therapy or prophylaxis.

Subgroups Most Likely to be Harmed:

Much less is known about the predictors of adverse effects of thromboprophylaxis than about efficacy, in large part because most of the patients at increased risk for complications related to the prophylaxis interventions were excluded from the clinical trials.

- Patients with an increased risk of bleeding with anticoagulant prophylaxis may include those with inherited or acquired bleeding disorders, patients with renal failure, the very elderly, those also taking antiplatelet agents, patients with a recent bleeding event, and those in whom primary hemostasis has not been achieved.
- Patients with a previous history of heparin-induced thrombocytopenia or who have been exposed to heparin within the past few months may be at increased risk for this complication related to prophylactic heparin exposure. Patient who have had proven heparin-induced thrombocytopenia should not be given a course of low-molecular-weight heparin because of the very high rate of at least in vitro cross-reactivity.
- Wound hematomas may be more prevalent in patients who commence anticoagulant prophylaxis before or shortly following surgery and in those with bleeding disorders.
- Although rare, the seriousness of perispinal hematoma mandates cautious use of antithrombotic medication in patients having neuraxial blockade. Increased awareness of this problem arose from observations made with low-molecular-weight heparin but it has also been reported with low-dose unfractionated heparin, although with apparent lower frequency. The benefit versus risk of any anticoagulant prophylaxis or therapy for patients with spinal/epidural anesthesia or analgesia is difficult to assess. Possible predictors of anticoagulant-related perispinal hematomas may include: history of a bleeding disorder, traumatic or very difficult epidural catheter insertion, and the dose of anticoagulant.

QUALIFYING STATEMENTS

Interpreting the Recommendations

The authors of these guidelines offer recommendations that should not be construed as dictates by the readers, including clinicians, third-party payers, institutional review committees, and courts. In general, anything other than a 1A recommendation indicates that the chapter authors acknowledge that other interpretations of the evidence and other clinical policies may be reasonable and appropriate. Even grade 1A recommendations will not apply to all circumstances and all patients. For instance, the guideline developers have been conservative in their considerations of cost, and have seldom downgraded recommendations from 1 to 2 on the basis of expense. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far more than some of the interventions that we designate grade 1A. This will likely be true for all less-industrialized countries. However, a weak recommendation (2C) that reduces resource consumption may be more strongly indicated in less-industrialized countries.

Similarly, following grade 1A recommendations will at times not serve the best interests of patients with atypical values or preferences. For instance, consider patients who find anticoagulant therapy extremely aversive, either because it interferes with their lifestyle (prevents participation in contact sports, for instance) or because of the need for monitoring. For such patients, clinicians may reasonably conclude that following some grade 1A recommendations for anticoagulation will be a mistake. The same may be true for patients with particular comorbidities (such as a recent gastrointestinal bleed or a balance disorder with repeated falls) or other special circumstances (such as very advanced age).

The guideline developers trust that these observations convey their acknowledgment that no guidelines or recommendations can take into account the often compelling idiosyncrasies of individual clinical circumstances. No clinician and no one charged with evaluating the actions of a clinician should attempt to apply their recommendations in a rote or blanket fashion.

Thromboprophylaxis

Although the guideline developers have attempted to provide an unbiased overview of the available data about thromboprophylaxis, they recognize that there are important limitations of the evidence largely due to the number and quality of the studies that form the basis for their recommendations. These caveats include the following points.

- Appropriate End Points for Studies of Deep Vein Thrombosis Prophylaxis:
  Physicians differ in their views on the appropriate end points for studies of deep vein thrombosis prophylaxis. The guideline developers suggest a middle ground based on large trials that use a clinically important venous

thromboembolism outcome, consisting of a composite of fatal pulmonary embolism, symptomatic, proven deep vein thrombosis or pulmonary embolism, and asymptomatic proximal deep vein thrombosis. These larger trials should be performed once smaller studies using an accurate test for all deep vein thrombosis have demonstrated the biological efficacy of the intervention.

- Limitations of Deep Vein Thrombosis Screening Methods:
  Each of the deep vein thrombosis screening methods has limitations. Despite the limitations, the relative risk reductions when two prophylaxis choices are compared using thromboembolism outcome measures are likely to be valid as long as systematic bias has been eliminated.
- Mechanical Methods of Prophylaxis:
  Special caution should specifically be exercised when interpreting the risk reductions ascribed to mechanical methods of prophylaxis for three reasons. Most trials have not been able to blind the mechanical devices, leading to the potential for diagnostic suspicion bias. If fibrinogen leg scanning was the deep vein thrombosis screening method, the known 10 to 30% false positive rate of the fibrinogen uptake test might have been reduced by the mechanical prophylaxis but not by the alternative option. Finally, because of relatively poor compliance with all mechanical options, they may well not perform as well in routine clinical practice as in research studies where major efforts are made to optimize proper use.
- Results May Not Apply to All Patients:
  Because most studies have excluded the patients at highest risk for both thromboembolic and adverse outcomes, the results may not apply to all patients, especially those with previous history of venous thromboembolism, or to patients with a greater-than-average bleeding potential.
- Prophylaxis Decisions for an Individual Patient:
  The prophylaxis recommendations contained herein are made for groups of patients, for whom the benefits appear to outweigh the risks. However, prophylaxis decisions for an individual patient are best made by combining knowledge of the literature (including the group recommendations provided herein and elsewhere) with clinical judgment (including detailed knowledge of that particular patient´s unique risks for thrombosis, the potential for adverse consequences due to the prophylaxis, and the availability of various prophylaxis options locally). The recommendations that are best for the group may not be best for the individual.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA Jr, Wheeler HB. Prevention of venous thromboembolism. Chest 2001 Jan;119(1 Suppl):132S-175S. [630 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

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American College of Chest Physicians Consensus Panel on Antithrombotic Therapy

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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GUIDELINE STATUS

Please note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

GUIDELINE AVAILABILITY

Electronic copies of the updated guideline: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Sixth ACCP Consensus Conference on Antithrombotic Therapy (2001): summary recommendations. Northbrook, IL: ACCP, 2001. (Quick reference guide for clinicians).

Electronic copies: Available from the American College of Chest Physicians Web site. (HTML, Portable Document Format [PDF], and downloadable files intended for use with Palm OS compatible devices are available.)

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348, or by calling 1 (800) 343-2227.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on July 12, 2001. The information was verified by the guideline developer on September 27, 2001.

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